## REMARKS

Claims 18-34 are pending. No new matter has been added.

### Finality of the Office Action

Applicants disagree with the characterization of the Office Action as a Final Office Action. No rejections are maintained from the previous Office action. It is suggested that the claim amendments necessitated the new rejection. This is not accurate. Claim 18 was amended to incorporate a limitation of a co-pending dependent claim. If the rejection is appropriate now, it should have been applied to the dependent claim in the first Action. No action on the part of the Applicant has caused this rejection to be raised for the first time in a Final Office Action. Applicants have not been afforded an adequate opportunity to address this new rejection. Therefore, it is respectfully requested that the finality of the Office Action be withdrawn.

### Rejection of Claims 18-34 Under 35 U.S.C. 112, First Paragraph

Claims 18-34 have been rejected under 35 U.S.C. 112, first paragraph, "as containing subject matter not described in a way as to reasonably convey to one of skill in the art that the inventors had possession of the claimed invention at the time the application was filed." The Examiner maintains that this is a new matter rejection as there is no support in the specification or claims as originally filed for the recitation of "...the isolated MBL binding peptide has an MBL binding $CDR3_1$ region or a functional variant thereof of a monoclonal antibody produced from a hybridoma cell line $_{(2A9)}$."

Applicants have amended claim 18 to fix a transposition error. Support for the amendment can be found in the specification on page 19, lines 23-29 which describes the CDR3 region or functional variant thereof of the monoclonal antibody produced by any of the three hybridoma cell lines. The correction of the inadvertent error in independent claim 18 is sufficient to overcome the rejection of these claims.

Claims 30-32 have been incorrectly included in this rejection. The rejection and arguments presented do not pertain to these claims as they are independent claims directed to the three deposited hybridoma cell lines.

**Rejection of Claims 18-34 Under 35 U.S.C. 112, First Paragraph**

Claims 18-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter not described in a way to reasonably convey to one of skill in the art that the Applicants, at the time the application was filed, had possession of the claimed invention. The Examiner maintains that the disclosure of the three antibodies does not adequately describe the scope of the claimed genus, namely "...any MBL inhibitor that has one of the three recited CDR3 regions or a functional variant thereof,...". It is the Examiner's position that the MBL binding peptide which comprises a CDR3 region or functional variant thereof can encompass an indeterminate number and kind of additional amino acids. Additionally, the functional variants of the recited CDR3 regions encompasses any number and combination of substitutions. Therefore, the Examiner concludes that since the prior art does not provide "structural or correlated teachings", one of the skill in the art is not enabled to identify the peptides of the claims and therefore would not recognize that the Applicant was in possession of "an isolated MBL binding peptide."

The specification thoroughly describes the structural and functional characteristics of the isolated MBL binding peptides as well as methods of making them. "Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure, and the method of making the claimed invention." (MPEP § 2163). Additionally, the level and knowledge of one of skill in the art is high.

The claimed invention relates to peptides which include a core piece having a biological activity. The invention is based on the discovery that the core peptide has an important functional property (MBL binding and inhibition). The claimed invention encompasses the core peptide with or without additional amino acids. A hybridoma producing an antibody from which the core peptide is derived has been deposited. One of skill in the art can access the hybridoma and obtain the core peptide that forms the basis of the invention. Functional variants of the core peptide do not encompass an indeterminate amount of amino acids. The specification provides adequate guidance for identifying functional variants. Only a limited number of changes can be made to the core peptide that result in modifications that qualify as functional variants. Additional amino acids can be added to the core peptide so long as they maintain the essential

structural and functional properties encompassed by the invention. The specification provides adequate guidance for accomplishing the claimed invention.

It is known to those of skill in the art, how to determine the sequence of a fragment of an antibody, synthesize and/or isolate a peptide, make functional variants and assess the ability of the peptides to perform a desired function. Additionally, the specification provides examples of such methods and thoroughly describes the functional characteristics of the MBL binding peptides. On page 13, the "isolated MBL binding peptide" is defined as a peptide which binds to MBL and inhibits LCP associated complement activation. The claims further limit the isolated MBL binding peptide to be based on the core CDR3 peptide of the deposited hybridoma or functional variants thereof. Functional variants and conservative substitutions are defined on pages 19-20. The specification further discloses methods for synthesizing these peptides, described on pages 15 and 26-27, as well as methods for determining binding to MBL and inhibition of LCP associated complement activation. Assays for assessing the inhibition of MBL deposition or association with MASP-1, MASP-2 and/or C3b are given on pages 11-12. On page 12-13, assays are given to assess the inhibition of LCP associated complement activation. Further examples include binding assays and competition assays described on pages 16-17 and activation assays on page 18.

The rejection and arguments presented do not pertain to claims 30-32 which are directed to the three hybridoma cell lines described in the specification and labeled with ATCC accession numbers HB-12621, HB-12620 and HB-12619.

**Rejection of Claims 18-34 Under 35 U.S.C. 112, First Paragraph**

The Examiner has rejected claims 18-34 under 35 U.S.C. 112, first paragraph, as not reasonably providing enablement for the recitation of a "composition comprising an MBL inhibitor comprising any peptide comprising an MBL CDR3 region of said antibodies or any functional derivative thereof." The Examiner further maintains that one of skill in the art would not be able to practice the invention as broadly as claimed without undue experimentation as the scope of the claims is not commensurate with the guidance provided by the disclosure due to the extremely large number of binding peptides encompassed by the claims. The Examiner argues

that it would not be predictable as to what changes would be tolerated in a peptide amino acid sequence and cites the teachings of Janeway et al., 1999 and Abaza et al., 1992.

Based on the knowledge in the art and the teachings of the specification, one of skill would know how to make a peptide comprising one of the three CDR3 regions of the antibodies produced from the deposited hybridoma cell lines. One of ordinary skill would also be able to determine whether or not a peptide possessed the desired functional characteristics. As set forth in the prior section, the specification provides a detailed description and examples demonstrating to one of skill in the art how to make and use the invention. The specification includes a description of the hybridomas, the core region of the hybridomas, methods for producing peptides and functional variants, screening assays, etc.

Further, the specification teaches the importance of the core CDR3 region for antibody specificity. In fact, the teachings of Janeway et al., 1999 do not argue against this. It is well known in the art that antibodies possess useful binding fragments. It is also known, as discussed above that one of skill would practice routine methods based on the knowledge of an antibody to make antibody fragments with a desired function. The specification provides the teachings that the sequence of a CDR3 region of a particular antibody can easily be determined by one of skill in the art (see page 27). With the sequence, one of skill would recognize how to synthesize peptides containing the CDR3 region. One of skill would also recognize that functional variants may also be produced and the specification provides adequate guidance to enable one of skill in the art to do so. This combination would allow one of skill in the art to make and synthesize the MBL binding peptides and variants thereof of the rejected claims. The claims do not cover any CDR3 region, but rather are limited to the CDR3 region of the antibodies produced by the deposited hybridomas. Additionally, the function of these peptides can be assessed with routine experimentation known in the art and described in the specification (see above). The teachings of Janeway et al., do not disprove the Applicants' assertion of the importance of the CDR3 binding region. Additionally, because of the high level of skill and knowledge in the art as well as the guidance provided in the specification, the Applicants assert that the specification is sufficient for making and assessing the effectiveness of the peptides which comprise this region.

Further, the teachings of Abaza et al. do not address the predictability of amino acid substitutions in an MBL binding peptide comprising a CDR3 region. Abaza et al. teaches single

amino acid changes in an antigen outside of its epitope. These teachings are not instructive with regard to amino acid changes in a CDR3 region of an antibody which, in fact, creates the antigen-binding site. Further, there is sufficient knowledge in the art and guidance provided in the disclosure for one of skill to know how to make substitutions in the peptides and determine the functionality of the variant peptides produced. Conservative substitutions are described in the specification on page 19.

Therefore, based on the guidance provided in the disclosure as well as the high level of knowledge and skill in the art, one would be able to make and use MBL binding peptides and functional variants thereof based on the antibodies produced by the Applicants' deposited hybridoma cell lines. The Applicants respectfully request the Examiner reconsider her rejection of these claims as the experimentation required is routine in the art and not undue.

## CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request that the Examiner withdraw the rejections. This application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes after this Amendment that the application is not in condition for allowance, the Examiner is requested to call the Applicants' attorney at the number requested below.

Respectfully submitted,

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## MARKED-UP CLAIMS

18. (Twice Amended) A composition, comprising an MBL inhibitor, wherein the MBL inhibitor is an isolated binding peptide that selectively binds to a human MBL epitope and that inhibits LCP associated complement activation, wherein the isolated MBL binding peptide has an MBL binding CDR3[$_1$] region or a functional variant thereof of a monoclonal antibody produced by a hybridoma cell line selected from the group consisting of hybridoma cell line$_{(3F8)}$ hybridoma cell line$_{(2A9)}$, and hybridoma cell line$_{(hMBL1.2)}$ deposited under ATCC accession numbers HB-12621, HB-12620, and HB-12619 respectively.